cartridge or inside the instrument. Such a fluid motive source may be provided by a pressurized (or evacuated) canister, chip, or other container. The motive source could also be a compressor or vacuum pump located either inside the cartridge or inside the instrument. In the instances in which an external pressure or vacuum motive source is used, the cartridge has suitable ports, vents, or channels for interfacing with the source. Likewise, electrophoretic or electroosmotic sources may be employed. Piezoelectrically, magnetically, or electrostatically driven membrane pumps or valves could also be incorporated into the cartridge or permanently installed in the instrument so that the devices are mechanically interfaced with the cartridge when the cartridge is inserted into the instrument.

[0067] In operation, a fluid sample containing a desired analyte, e.g. nucleic acid, is added to the sample port **103** of the cartridge **101** and forced to flow continuously (such as with an electrolytic or mechanical pump) down a channel **105** and into the mixing chamber **107**. Lysing reagents are simultaneously released from the storage chamber **109** and forced to flow down a channel **111** and into the chamber **107**. Suitable lysing reagents include, for example, solutions containing a chaotropic salt, such as guanidine HCl, guanidine thiocyanate, guanidine isothiocyanate, sodium iodide, urea, sodium perchlorate, and potassium bromide.

[0068] The fluid sample and lysing reagents traveling in the channels **105** and **111**, respectively, are detected by resistive sensors **115**. As the lysing reagent contacts the fluid sample, cells, spores, or microorganisms present in the fluid sample begin to be lysed. The fluid sample and lysing reagent continue to flow into the lysing chamber **119** where the sample contacts a filter and the cells, spores, or microorganisms are captured. The lysing reagent continues to lyse the captured sample components. The filter also serves to remove debris from the fluid sample.

In another important embodiment of the invention, an ultrasonic transducer is coupled to the cartridge **101** next to lysing chamber **119**, e.g. coupled to a wall of the chamber **119**, and the sample components are lysed by ultrasonic energy provided by the transducer. Various ultrasonic lysing embodiments are discussed in greater detail below with reference to FIGS. **19-20**.

[0069] The lysed sample proceeds from the lysing chamber **119** down channel **121** and is forced to flow through the capture component **122**. As the fluid sample and lysing reagent flow through the component **122**, nucleic acid in the fluid sample binds to the component **122**. The flow-rate of the fluid sample through the component **122** is preferably in the range of 0.1 to 50 μL/sec. The fluid sample and lysing reagent exiting the component **122** flow down channel **135**, through the flow controller **41**A, and through channel **136** to the waste chamber **139**. In another embodiment, after flowing through the component **122**, the fluid sample may be redirected to recirculate through the component additional times.

[0070] After the fluid sample is forced to flow through the component **122**, the washing reagent in storage region **125** is forced to flow down a channel **129** and through the component **122**. The wash flow rate is preferably on the range of 0.5 to 50 μL/sec. Fluid is prevented from flowing upstream in the cartridge by flow controllers **123** in channels **121**, **129**, and **131**. The washing reagent washes residual contaminants, such as chaotropic salts, from the component **122**. A variety of suitable wash solutions of varying pH, solvent composition, and ionic strength may be used for this purpose and are well known in the art. For example, a suitable washing reagent is a solution of 80 mM potassium acetate, 8.3 mM Tris-HCl, pH 7.5, 40 uM EDTA, and 55% ethanol. The washing reagent continues to flow through the flow controller **41**A and into the waste chamber **139**.

[0071] After washing the component **122**, elution fluid from the storage region **127** is forced to flow down channel **131** and through the component **122**, thus releasing the nucleic acid from the component into the elution fluid. At this point, the flow controllers **41**A and **41**B are reconfigured to prevent the elution fluid from flowing through the flow controller **41**A and to permit the elution fluid to flow through the flow controller **41**B into the reagent chamber **141**. The flow rate of elution fluid through the component **122** is preferably in the range of 0.1 to 10 μL/sec. The flow rate of the elution fluid may be relatively slow as compared to the flow rate of the fluid sample to allow for more analyte to be released from the component.

[0072] In general, any suitable elution fluid may be used to elute nucleic acid from the component **122**. Such elution fluids are well known in the art. For example, the elution fluid may comprise molecular grade pure water, or alternatively, a buffer solution, including but not limited to a solution of TRIS/EDTA; TRIS/acetate/EDTA, for example 4 mM Tris-acetate (pH 7.8), 0.1 mM EDTA, and 50 mM NaCl; TRIS/borate; TRIS/borate/EDTA; potassium phosphate/DMSO/glycerol; NaCl/TRIS/EDTA; NaCl/TRIS/EDTA/TWEEN; TRIS/NaCl/TWEEN; phosphate buffers; TRIS buffers; HEPES buffers; nucleic acid amplification buffers; nucleic acid hybridization buffers, etc.

[0073] Prior to forcing the elution fluid to flow through the component **122**, an intermediate air-gap step may optionally be performed. A gas, preferably air, may be forced to flow through component **122** after the wash solution flows through and before the elution fluid flows through. The air-gap step provides for clear separation of liquid phases, and helps at least substantially dry the component **122** of any remaining wash solution prior to elution.

[0074] The component **122** is preferably heated as the elution fluid is forced to flow through it to increase elution efficiency. The heating is preferably performed by supplying power to a resistive heating element in a closed loop feedback system under the control of the processing electronics in the cartridge. In the preferred embodiment, the component **122** is heated to a temperature in the range of 60 to 95° C. as the elution fluid flows through the it.

[0075] Elution fluid containing the nucleic acid exits the component **122** and travels down the channel **135** to the reagent chamber **141**. The elution fluid and nucleic acid contact and reconstitute dried PCR reagents contained in the chamber **141**, and the elution fluid, nucleic acid, and PCR reagents continue to flow into reaction chamber **143** for PCR amplification and detection. In an alternative embodiment, the elution solution already includes PCR reagents so that the reagent need not be dried in the chamber **141**. Vents **145** in communication with the waste chamber **139** and the reaction chamber **143** allow release of gases during the process.

[0076] One advantage of the continuous-flow cartridge of the preferred embodiment is that it allows the analyte, e.g. nucleic acid, from a relatively large volume of fluid sample, e.g. several milliliters or more, to be concentrated into a much smaller volume of elution fluid, e.g., 25 μL or less. In contrast to prior art devices, the cartridge of the present invention permits extraordinary concentration factors by efficiently